

REMARKS/ARGUMENTS

Claims 1-37 are active in this application.

The claims have been amended in response to the finality of the imposed Restriction Requirement where X is S or O; Y¹ is S or O; and Y² is S or O. Non-elected species are retained as reconsideration of that election is still ongoing (see pages 2-3 of the Official Action)

The remaining changes are simply for clarity.

No new matter is added.

The sole substantive rejection is that the claims are not enabled for the prophylaxis and/or treatment of the diseases listed in the claims. Specifically, the Examiner's allegation is that there is little data in the specification which would support that these types of compounds would be effective for the prophylaxis and/or treatment of all diseases and/or disorders encompassed by the claims.

Applicants disagree.

The claims of this application based on the use of compound according to formula I which are azolidinone-vinyl fused-benzenes. The listing of diseases is described in the specification as linked to the activity with the PI3k lipid kinase. Indeed the specification in the Background section of the invention provides a lengthy discussion as to how the PI3k functions as well as its involvement in cell signal. For example, on page 6 of the application there is a correlation of PI3k activity and acute/chronic inflammation.

Since the target P13K is a well-validated target in pharmaceutical research the compounds and its use in the diseases claimed is clearly enabled.

This holds true even in the absence of specific dose regimens for treatment or prophylaxis. Considering the significance of the finding of a group of compounds that are active on P13K, it appears not well balanced that the applicant is required to provide all details of the administration. Further, it is routine in the medical field to optimize dosages based on the disease, severity, gender, race, age among a host of other factors facing the individual patient.

Thus, further experimentation cannot be considered an undue burden.

Applicants submit a number of documents that clearly support the fact that the target P13K is effective for the treatment of the diseases claimed. That is, as P13K is an effective target for treating the diseases identified in the claims and that the specification provides evidence that the azolidinone-vinyl fused-benzenes defined in the claims modulate the P13K activity provides the necessary enabling disclosure of the methods as claimed in this application.

Neutropil cell signaling in infection or Infection:

Downey et al. *Microbes and Infection* 5 (2003), 1293-1 298.

Weinstein et al. *Journal of Leucocyte Biology* volume 67, March 2000, 405-414.

Inflammation and allergy:

Wymann et al. *Biochemical Society Transactions* (2003) volume 31 Part 1, 275-280.

Regulation of intestinal Epithelial cells:

Sheng et al. *Gut* 2003 52: 1472-1478.

Heart diseases:

Nienaber et al. *The Journal of Clinical Investigation* October 2003 volume 112 Number 7, 1067-1079.

Cancer diseases:

Sawyers et al. *Nature Review Cancer* volume 2 July 2002, 489-501.

Brennan et al. *Oncogene* 2002, 21, 1263-1 271.

Roche et al. *Oncogene* 2000, 19, 5083-5090.

Wetzker et al. *Cell Growth and Differentiation*, vol.10, 447-456, June 1999.

Ward et al. *Trends in Molecular Medecine* vol.7, Nol 0. October 2001, pp 455-462.

Inflammatory:

Weaver et al. *Gastroenterology* 2001, 120, 1117-1127.

Chock et al. *PNAS*, June 20, 2000, vol.97, no.13, 71 18-7123.

Kita et al. *FEBS Letters* 441(1998) 63-66.

Yano et al. *Biochem. J.* 1995, 312, 145-1 50.

Vascular diseases:

Hirsch et al. *The Faseb Journal* vol.15 September2001, 2019-2021.

Vogt et al. *PNAS*, February 15, 2000, vol.97, no.4, 1749-1 753.

T-cell Activation and Lymphocytes:

Fresno et al. *The Journal of Biological Chemistry* vol 276, No 19, Issue of May 11, 2001, pp 15840-1 5849.

Johnson et al. *Proc. Natl. Acad. Sci, U.S.A.* vol.94, pp 3052-3057. April 1997.

Hirai et al. *Oncogene* 1997, 14, 3067-3072.

Thelen et al. *Biochemical and Biophysical Research Communications*, vol. 217, No.3, 1995, pp 1255-1262.

Bierer et al. *Proc. Natl. Acad. Sci., USA* vol. 92, pp 8808-881 2. September 1995,

Apoptosis:

Benjamin et al. *Journal of Virology*. Apr 1998, pp 3221-3226.

Asthma:

Plevin et al. *Biochem. J.* 1996, 318, pp 965-971.